IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Zhangdong, et al.
Title:	COMPOSITIONS AND METHODS FOR DETECTING REVERSE TRANSCRIPTASE IN A SAMPLE
Appl. No.:	10/750,092
Filing Date:	December 31, 2003
Examiner:	Baughman, M.E.
Art Unit:	1637
Confirmation Number:	1890

PRE-APPEAL BRIEF REQUEST FOR REVIEW

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Commissioner for Patents
P.O. Box 1450
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Sir:

In accordance with the Pre-Appeal Brief Conference Pilot Program, this Pre-Appeal Brief Request is being filed together with a Notice of Appeal.

REMARKS

Claims 28 and 53 are the pending independent claims. Each encompasses a kit with components useful for detecting reverse transcriptase enzymatic activity in a sample. Each claimed kit requires the presence of "a deoxynucleoside triphosphate labeled with an acridinium moiety." The Examiner has failed to provide a prior art reference that utilizes this moiety for any purpose, let alone in the context of a reverse transcriptase enzymatic assay kit.

Rejection Under 35 U.S.C. § 103(a)

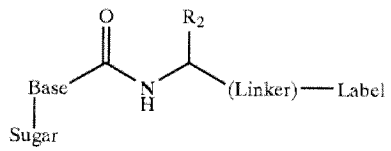
The Examiner rejects all pending claims over the combination of Eberie et al. (U.S. Patent 5,413,906) and Bodepudi et al. (U.S. Patent Publication 2004/0171040), alone or in further combination with either Petrie et al. (U.S. Patent 5,824,796) or Nelson et al. (Biochemistry, 35: 8429-8438, 1996). Applicants strongly disagree with the Examiner's interpretation of Bodepudi et al. and urge that a favorable interpretation of Bodepudi et al. is dispositive for all rejections.

Eberie et al. in view of Bodepudi et al.

Applicants traverse the rejection of claims 28-30, 40-43, 45-46, 53-59, 61-65, and 68 as obvious over Eberie et al. in view of Bodepudi et al.

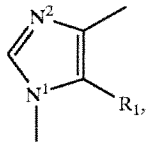
The Examiner alleges that Eberie et al. teach a kit containing substantially the same reagents as required in Applicants' claimed invention. Final Office Action mailed March 30, 2007, at p. 3, ¶ 4. The Examiner acknowledges, however, that Eberie et al. do not teach deoxynucleoside triphosphates (dNTPs) labeled with an acridinium moiety. Final Office Action at p. 4, ¶ 1. To remedy this deficiency, the Examiner alleges that Bodepudi et al. teach acridinium-labeled dNTPs and that it would have been obvious to use these labeled dNTPs in the kit of Eberie et al. Final Office Action, at p. 5, ¶ 1. Applicants strongly disagree with the Examiner's characterization of Bodepudi et al.

In contrast to the Examiner's belief, Bodepudi et al. do not teach acridinium-labeled dNTPs. In fact, the only acridinium-labeled compounds taught by Bodepudi et al. are non-purine and non-pyrimidine dNTP derivatives. Specifically, Bodepudi et al. provide labeled compounds having the following generic structure (Boudepudi et al. at ¶¶ 7, 16, 26, 60, 136, 145, 218, and 228):



(I).

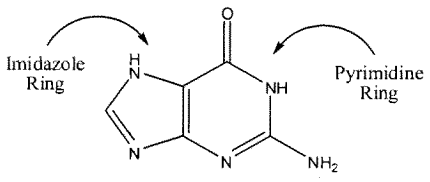
For each and every instance in which Boudepudi et al. provide a generic chemical structure containing a "Base" moiety, "Base" is immediately and invariably defined as having the following structure:



(II),

wherein R_1 is " H, $HNC(O)NH_2$, NH_2, OH, O(alkyl), alkyl, CO_2H (see, for example, Boudepudi et al. at ¶¶ 10-12).

The "Base" of Compounds (I) and (II) clearly excludes a dNTP (i.e., a nucleobase) by any definition. dNTPs (nucleobases) are art recognized as having either a purine structure or a pyrimidine structure. Compound (II) contains neither. For the Examiner's convenience, the chemical structure of guanine, a purine, is provided below as Compound (III).



(III)

Boudepudi et al.'s Compound (II) contains an imidazole ring, similar to that contained in the purine bases (e.g., adenine and guanine) but, Boudepudi et al. never suggest a configuration of R_1 which forms a pyrimidine ring necessary for a properly formed purine base. For specific examples of the nucleobase derivatives provided by Boudepudi et al., Applicants respectfully direct the Committee's attention to the compounds at ¶¶ 171, 175, 178, 181, 185, 188, 191, 194, 197, 200, 202, 204, 206, 208, 210, 212, 214, 216, 257, 261, 264, 267, 271, 274, 277, 281, 284, 287, 289, 291, 293, 295, 297, 299, 301, and 303. None of these compounds contain a nucleobase structure because the R_1 group is never cyclized into a pyrimidine ring (or any ring structure). Thus, Compound (II) is never disclosed as being a dNTP (nucleobase). Accordingly, the inventive acridinium-labeled compounds of Boudipudi et al. cannot be properly combined with the assay of Eberie et al. to render obvious Applicants' claimed invention.

In maintaining this rejection, the Examiner points to the boilerplate definitions of "nucleobase" and "nucleobase analog" (¶¶ 98-99) and alleges that Boudepudi et al. suggest

labeling these compounds with acridinium. Advisory Action mailed July 19, 2007 at ¶ 3; Final Office Action at p. 4, ¶ 2. This allegation is false. Boudepudi et al. never suggest labeling the nucleobases or nucleobase analogs, as defined in ¶¶ 98-99, with acridinium. Furthermore, the Examiner has failed to connect the boilerplate definitions of unlabeled nucleobase and nucleobase analogs to the inventive acridinium-labeled compounds disclosed by Boudepudi et al.

Boudepudi et al. define "nucleobases" as being limited to the naturally-occurring purine and pyrimidine based found in DNA and RNA; adenine, cytidine, guanine, thymine, and uracil. Boudepudi et al. at ¶ 98. Nothing in Boudepudi et al. suggests labeling nucleobases with an acridinium moiety.

Moreover, nothing in Boudepudi et al. suggests labeling nucleobase analogs with an acridinium moiety. "Nucleobase analogs" are defined by Boudepudi et al. as including substituted or unsubstituted nitrogen-containing parent heteroaromatic rings. Boudepudi et al. at ¶ 99. The inventive compounds cannot be nucleobase analogs, as defined therein, because they do not contain a parent heteroaromatic ring (i.e., purine or pyrimidine ring structures). This interpretation is supported by the preferred nucleobase analogs identified in the definition which include purines, deazapurines, and pyrimidines. Id. The definition is further exemplified with at least 24 specific nucleobase analogs, all of which fail to conform to the generic structure of Compound (II). Thus, the inventive compounds (which are the only compounds suggested as containing an acridinium label) clearly do not fall within Boudepudi's definition of nucleobase and nucleobase analogs. It is clear that Boudipudi et al. considered the inventive acridinium-labeled compounds as separate and distinct chemical entities from nucleobases as well as nucleobase analogs.

Applicants' claimed invention requires the use of acridinium labeled dNTPs. Applicants' required dNTPs are clearly different from the acridinium-labeled compounds of Boudipudi et al. which are defined by Compound (I).

In sum, Boudipudi et al. provide acridinium-labeled compounds conforming to the generic structure of Compound (I). Compound (I) is not a nucleobase or a nucleobase analog, as defined therein. Boudipudi et al. at ¶¶ 98-99. Thus, contrary to the Examiner's assertion, Boudipudi et al. never teach or suggest an acridinium-labeled nucleobase or nucleobase analog. The Examiner has further failed to demonstrate how the boilerplate definitions of nucleobase and

nucleobase analogs relate to the inventive acridinium-labeled compounds disclosed by Boudepudi et al. And, the Examiner has failed to demonstrate a specific suggestion by Boudepudi et al. to make an acridinium labeled nucleobase. Accordingly, because the acridinium-labeled compounds of Boudipudi et al. are not acridinium-labeled nucleobases (dNTPs), the combination of Boudipudi et al. with Eberie et al. fails to render obvious Applicants' claimed invention. This rejection is traversed and should be withdrawn.

Eberie et al. in view of Bodepudi et al. and either Petrie et al. or Nelson et al.

Claims 44, 47-51, 60, and 63-67 stand rejected as obvious over of the combination of Eberie et al. and Bodepudi et al. in further view of either Petrie et al. or Nelson et al. Applicant respectfully traverses these rejections.

The Examiner asserts Petrie et al. as providing chemical linkers to attach the dNTP to the acridinium label. Final Office Action at p. 6, ¶ 2. The Examiner asserts Nelson et al. as providing oligomeric probes labeled with various acridinium esters. Final Office Action at p. 8, ¶ 1. Neither of these secondary references remedy the deficiencies of the basic combination of Eberie et al. and Bodepudi et al.—the lack of an acridinium-labeled dNTP in a kit for detecting reverse transcriptase activity in a sample. Accordingly, these rejections are also traversed and should be withdrawn.

In view of the foregoing, it is respectfully submitted that the application is in condition for allowance and such action is respectfully requested.

Respectfully submitted,

Date 08/30/2007

By _____

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